REMARKS

Claims 1-14 are currently pending in this application and and claims 10-14 are withdrawn from consideration.

Rejections under 35 USC 103(a):

The Examiner rejected claims 1-9 under 35 U.S.C. § 103(a), as allegedly unpatentable over Garvey *et al.* (US 5,824,669) ("Garvey") in view of Carling *et al.* (US 5,674,860) ("Carling") and Palmer (US 5,208,226) ("Palmer").

In response, applicants respectfully traverse the Examiner's rejections under 35 U.S.C. § 103(a) and maintain that the Examiner has failed to establish a *prima facie* case of obviousness against the instant invention. Currently, to establish a *prima facie* case, the PTO must satisfy three requirements:

1) **the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references**. *See Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376, 1385, 58 U.S.P.Q.2d 1286, 1293 (Fed. Cir. 2001) ("In holding an invention obvious in view of a combination of references, there must be some suggestion, motivation, or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would produce the claimed invention."); *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352, 48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998) (a showing of a suggestion, teaching, or motivation to combine the prior art references is an "essential evidentiary component of an obviousness holding"). *Northern Telecom v. Datapoint Corp.*, 908 F.2d 931, 934, 15 U.S.P.Q.2d 1321, 1323 (Fed. Cir. 1990) (It is insufficient that the prior art disclosed the components of the patented

device, either separately or used in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by the inventor."); *Abbott Laboratories v. Syntron Bioresearch, Inc.*, 334 F.3d 1343, 67 U.S.P.Q.2d 1337 (Fed. Cir.), *reh'g denied*, 2003 U.S. App. LEXIS 17605 (2003)("Knowledge in the prior art of every element of a patent claim, however, is not of itself sufficient to render claim obvious. The issue is whether substantial evidence supports the judgment (under the clear and convincing evidence standard) that a person having ordinary skill in the art would not have been motivated to replace the [prior art process] with [the process of the invention].");

2) **the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made**. In other words, a hindsight analysis is not allowed. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991) (While the idea of using a monkey gene to probe for a homologous human gene may have been "obvious to try," many pitfalls existed that would have eliminated a reasonable expectation of successfully obtaining the EPO gene. "Hindsight is not a justifiable basis on which to find that ultimate achievement of a long sought and difficult scientific goal was obvious."); and

3) **the prior art reference or combination of references must teach or suggest all the limitations of the claims**. *See In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art.").

Neither Garvey, Carling, or Palmer alone or in combination, renders the combination of long-lasting anticholinergics and long-lasting β-mimetics obvious, however, since none of the cited references, alone or in combination discloses, suggests, or even hints to one of skill in the art, much less with the required reasonable expectation of success, of the combination of long-lasting anticholinergics and long-lasting β-mimetics. Furthermore, neither Garvey, Carling, or Palmer teach, suggest, or even hint that the combination of long-lasting anticholinergics and

long-lasting β-mimetics provides a synergistic effect, that is, the effect provided by the claimed combination surprisingly exceeds the effect that would be expected from the addition of the effects provided by long-lasting anticholinergics and long-lasting β-mimetics individually. The references and rejections are addressed in more detail below.

In column 2, line 12, Garvey merely lists, "[v]arious categories of drugs known to be useful in the inhalation of treatment of asthma", of which ipratropium, tiotropium, and flutropium are just three of the compounds listed. Garvey claims, "[t]he present invention is based on the discovery by the inventors that it is possible to directly or indirectly link an NO or NO_2 group or a group which stimulates the endogenous production of NO or endothelium-derived relaxing factor (EDRF) in vivo, to a steroid, a β-agonist, an anticholinergic, a mast cell stabilizer or a phosphodiesteras (PDE) inhibitor and that the resulting compound has beneficial therapeutic effects of both a steroid, a β-agonist, an anticholinergic, a mast cell stabilizer, or PDE inhibitor and an NO donor or stimulator. (column 2, lines 55-62).

Nowhere does Garvey even suggest combining any of the listed compounds with anything other than an NO or NO_2 group.

Carling provides that two drugs, formoterol and budesonide, may be administered simultaneously, sequentially, or separately to provide a greater efficiency and duration of bronchodilator action with a rapid onset of action. (column 2, lines 33-39).

Palmer discloses, "combination therapy which has greater efficiency and duration of bronchodilator action than previously known combinations and which permits the establishment of a twice daily (bis in diem – b.i.d.) dosing regimen with consequent benefits in, for example, the treatment of asthma, particularly nocturnal asthma." (column 1, lines 62-68).

Carling, Palmer, or Garvey do not suggest the combination of anticholinergic and betamimetic compounds of this invention. Nor do Carling, Palmer, or Garvey do not disclose the unexpected result of this invention, that being the addition of an anticholinergic to a

betamimetic would act synerginistically to reduce the cardiac side effects of the betamimetic. (Tables on pages 16-21 of the specification).

In making this rejection, the Examiner has merely made conclusory statements about combining Carling, Palmer, or Garvey to obtain the instant claimed invention instead of providing the necessary analysis of obviousness. The fact that Carling, Palmer, or Garvey contain elements of applicants' claimed invention alone does not render the claimed invention obvious. Rejecting claims solely by finding prior art corollaries for the claimed elements would permit an Examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention, which is an illogical and inappropriate process by which to determine patentability. *Sensonics, Inc. v. Aerosonic Corp.*, 38 U.S.P.Q.2d 1551, 1554 (Fed. Cir. 1996); *In re Rouffet*, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998). Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion or incentive to do so. *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984). Indeed, as pointed out above, Rees provides a disincentive to do so. Virtually all inventions are combinations of old elements. *Environmental Designs, Ltd. v. Union Oil Co.*, 218 U.S.P.Q. 865, 870 (Fed. Cir. 1983). Thus, the mere mention of the classes of active ingredients in separate references does not alone render obvious their combination. The Examiner has not articulated the elements necessary to establish a *prima facie* case of obviousness against the instant invention using Carling, Palmer, or Garvey.

Applicants maintain that the above remarks and amendments overcome the Examiner's rejections and objections or render the Examiner's rejections and objections moot. Applicants therefore submit that all the pending claims are allowable and respectfully solicit a Notice of Allowance for all of the pending claims. If the Examiner feels that a telephone interview would be helpful in advancing prosecution of this application, the Examiner is invited to contact the attorney below.

Obviousness-type Double Patenting:

Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatenable over claims 1-15 and 1-5 of US 6,455,524 and 6,630,466 respectively.

In an effort to conclude prosecution, applicants herewith undertake to file a terminal disclaimer to overcome the nonstatutory obviousness-type double patenting rejection over US 6,455,524 and 6,630,466, at the conclusion of prosecution of this case, should that become necessary.

In view of the above amendments and remarks, Applicants respectfully submit that this application is now in condition for allowance and earnestly request such action.

If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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